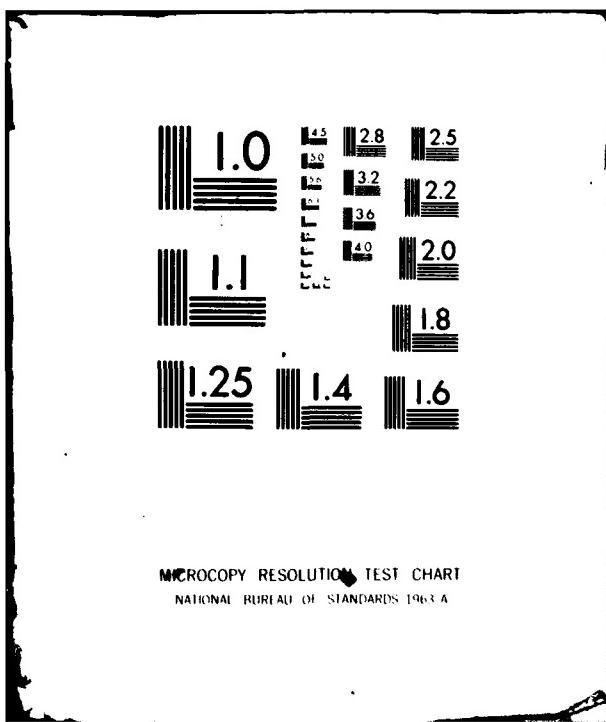


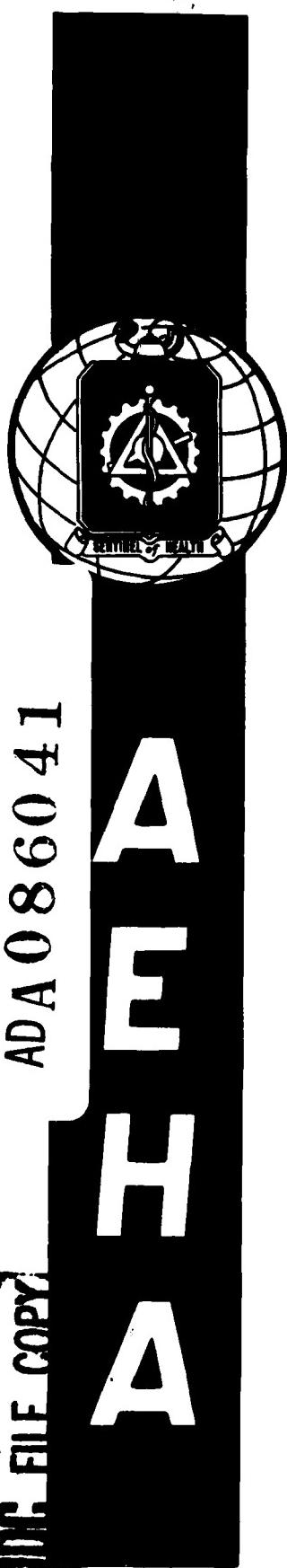
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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)  
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UNITED STATES ARMY  
ENVIRONMENTAL HYGIENE  
AGENCY

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM  
OF CANDIDATE INSECT REPELLENTS  
AI3-34155, 1-(4-CHLOROPHOXY)-2-(2-METHOXYETHOXY)-ETHANE AND  
AI3-34156, 1-(4-CHLOROPHOXY)-2-(2-ETHOXYETHOXY)-ETHANE  
STUDY NOS. 75-51-0015-80 AND 75-51-0016-80  
FEBRUARY 1977 - APRIL 1980

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-34155, 1-(4-chlorophenoxy)-2-(2-methoxyethoxy)-ethane, and AI3-34156 1-(4-chlorophenoxy)-2-(2-ethoxyethoxy)-ethane; study		5. TYPE OF REPORT & PERIOD COVERED Final, Feb 77 - Apr 80
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Preliminary hazard evaluations of AI3-34155 and AI3-34156 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compounds did not cause skin, eye, or photo irritation. They did not prove to be skin sensitizers or to be acutely toxic by ingestion. It was recommended that both compounds be approved for further testing as candidate insect repellents.		

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DEPARTMENT OF THE ARMY      CPT Singer/lm/AUTOVON  
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY      584-3980  
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT-T/WP

17 JUN 1980

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents  
AI3-34155, 1-(4-chlorophenoxy)-2-(2-methoxyethoxy)-ethane, and  
AI3-34156, 1-(4-chlorophenoxy)-2-(2-ethoxyethoxy)-ethane, Study  
Nos. 75-51-0015-80 and 75-51-0016-80, February 1977 - April 1980

Executive Secretary  
Armed Forces Pest Management Board  
Forest Glen Section, WRAMC  
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

Preliminary hazard evaluations of AI3-34155 and AI3-34156 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compounds did not cause skin, eye, or photo irritation. They did not prove to be skin sensitizers or to be acutely toxic by ingestion. It was recommended that both compounds be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

JOHN F. MAZUR  
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Director, Laboratory Services

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USDA, ARS (Dr. Terrence McGovern)  
USDA, ARS-Southern Region

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DEPARTMENT OF THE ARMY  
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY  
ABERDEEN PROVING GROUND, MARYLAND 21010

TOPICAL HAZARD EVALUATION PROGRAM  
OF CANDIDATE INSECT REPELLENTS  
AI3-34155, 1-(4-CHLOROPHOXY)-2-(2-METHOXYETHOXY)-ETHANE and  
AI3-34156, 1-(4-CHLOROPHOXY)-2-(2-ETHOXYETHOXY)-ETHANE  
STUDY NOS. 75-51-0015-80 and 75-51-0016-80  
FEBRUARY 1977 - APRIL 1980

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 10 February 1977.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administration, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEEHA), 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-34155 and AI3-34156.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate repellents AI3-34155 and AI3-34156 were conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:<sup>\*†</sup>

\* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1978.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Compounds AI3-34155 and AI3-34156 did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix).
0.5 mL technical grade compound applied to each of six rabbits.		
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade compound to one eye of each of six New Zealand White Rabbits.	Compounds AI3-34155 and AI3-34156 did not cause any irritation to the eyes of rabbits.	USAEHA Category A (ref Appendix).
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male)-no diluent	For AI3-34155, the ALD was determined to be 1125 mg/kg. For AI3-34156, the ALD was 3300 mg/kg.	Neither compound presents much lethal hazard from accidental ingestion.

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Test	Results	Interpretation
<u>PHOTOCHEMICAL SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
	A single 0.05 mL application of a 25 percent (w/v) solution of each compound and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	Neither compound in ethanol caused a photochemical irritation reaction under test conditions.
		Compounds AI3-34155 and AI3-34156 did not cause a photochemical irritation reaction under test conditions and are not expected to cause a photochemical irritation in humans.
<u>Control</u>		
	Following UV exposures of the rabbits, 0.05 mL of test compound, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.	Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.

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Test	Results	Interpretation
<b><u>SENSITIZATION STUDIES</u></b>		
<b><u>Guinea Pigs (Male)</u></b>		
Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-34155, AI3-34156 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs for each compound were given ten sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of each test compound.	Challenge doses of AI3-34155 and AI3-34156 did not produce a sensitization reaction.	Compounds AI3-34155 and AI3-34156 did not produce sensitization reactions under test conditions and are not expected to produce sensitization reactions in man.
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.

\* A known skin sensitizer

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5. CONCLUSION. Technical grade compounds AI3-34155 and AI3-34156 did not cause any skin, eye, or photo irritation, no sensitization reaction, and did not prove to be an acute ingestion hazard.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-34155 and AI3-34156 be approved for further testing as candidate insect repellents.

*Allen W. Singer*

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APPROVED:

*Arthur H. McCresh*

ARTHUR H. McCRESH, Ph.D.  
Chief, Toxicology Division

TOPICAL HAZARD EVALUATION PROGRAM  
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING  
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

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